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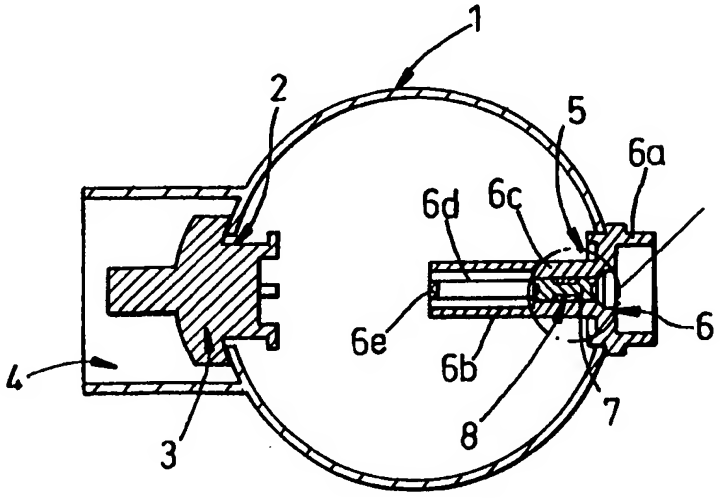
(54) Title: DRY POWDER AEROSOL PRODUCTION

(57) Abstract

A device for producing an aerosol of a micronised powder includes a chamber (1) having openable closure means (2, 3) which are operable to allow at least a partial vacuum to be created and maintained within the chamber. The device further includes means (5, 6, 7, 8), for introducing substantially simultaneously into the at least partially evacuated chamber both a measured quantity of powder and a gas so that an aerosol is formed within the chamber. The chamber is also provided with aerosol exit means whereby the aerosol may be withdrawn from the chamber. The invention also provides an associated method for producing an aerosol of a micronised powder.



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DRY POWDER AEROSOL PRODUCTION

FIELD OF THE INVENTION

This invention relates to a method and apparatus for producing an aerosol of a dry, micronised powder. More especially, it is concerned with medical inhalers in which a medicinal substance forms at least part of the micronised powder. The medicinal substance may be for use in the treatment of diseases of the respiratory tract.

BACKGROUND TO THE INVENTION

Devices for the production of an aerosol from a pulverulent substance have previously been disclosed. It is particularly desirable that the use of propellants, particularly those prejudicial to the environment, should be avoided. A propellant-free inhaler is disclosed in DE-A1-4027390, wherein a medicinal substance is accommodated in powder form in a storage container. A dose of the powder is removed by means of a dosing device, prior to the fitting of a mouthpiece, and thereafter the substance is entrained by the air flow which results from an act of inhalation by the patient. An air chamber is situated in the resulting air flow in order to distribute the substance therein and provide inhalable particles. However, the particle size achieved is largely dependent upon the nature and intensity of inhalation by the patient and, consequently, it is difficult to ensure consistency of treatment when using this device; in particular, the presence of sufficient, adequately small particles cannot be guaranteed. Thus, it is found that the process is not suitable for mass production, since it is not possible to produce the medicinal substance in a standard form for use by all patients.

A further propellant-free inhaler is disclosed in DE-A1-4027391, in which the problem of reproducibility is addressed by providing a cylinder containing a volume of air which is automatically released through a nozzle as a result of the action of breathing-in, and thereby provides an active air flow which ensures consistency in the provision of inhalable particles to the patient. Unfortunately, however, technical

difficulties associated with the requirement for the release of a precise quantity of air result in a system which is both difficult and expensive to produce.

Generally, in the known art, there are many examples of devices which suffer from the difficulties associated with the provision of an aerosol having a consistent and reproducible particle spectrum and mist density. Such features are inevitably dependent upon the ability to accurately deliver a precise airflow to the pulverulent substance. In an effort to overcome these difficulties a device is disclosed in WO-A-90/07351 in which the airflow is generated by means of a pressurised gas source or a piston/cylinder arrangement and fed via a nozzle in order that a controlled flow rate may be achieved. When approaching the maximum flow rate, a duct is opened into the flow path, providing a connection to a storage vessel containing the pulverulent substance, which is thereby sucked into the airflow and conveyed into a mixing chamber in order to achieve a good distribution of particles therein. However, since the preparation of the aerosol takes place completely independently of the inhalation of the patient, and an active airflow is directed into the respiratory tract of the patient, it is generally not possible to achieve a good particle distribution both before and during inhalation.

Devices for the production of high density aerosols containing relatively small and inhalable particles have been disclosed in EP-B-0667793 and EP-A1-0722746, wherein a precisely defined volume of pulverulent material is introduced as a bed of dry powder into a chamber of predetermined volume, said chamber then being at least partially evacuated prior to allowing a gas to flow therein, thereby causing the pulverulent substance to whirl up into an aerosol, a predetermined volume of which may then be forced from the chamber. Following release of the vacuum, the heavier particles of the pulverulent substance should fall back to the powder bed whilst the smaller, deagglomerated micronised particles remain for a relatively long time in the aerosol, this being inhaled by the user after exit from the chamber.

However, whilst arrangements of this type produce high quality aerosols which are high in particles of respirable fraction, various drawbacks are encountered during routine use of the devices for the delivery of drugs. In particular, difficulties are associated with the manner in which the medicant, in dry powder form, is contained in the device and the amount of medicant required to produce a number of reproducible and consistent results in terms of quantity and quality of aerosol. The arrangement requires that a bed of powder is provided and, in certain instances, the situation is unsatisfactory since the amount of micronised powder required to form the bed may have to be 2 to 3 times the total amount expected to be administered from the device in the form of inhalable aerosol. Furthermore, with multi-dose devices, it is often not appropriate to store certain drugs in such a bulk fashion for a length of time within the device.

Consequently, it is an objective of the present invention to provide a method and device for producing an aerosol of a micronised powder, which method and device overcome the difficulties associated with such bulk storage of a pulverulent substance, in particular a medicament, whilst at the same time retaining the advantages which result from the use of a vacuum-type system.

STATEMENTS OF INVENTION

According to the present invention, there is provided a device for producing an aerosol of a micronised powder, said device comprising a chamber having openable closure means operable to allow at least a partial vacuum to be created and maintained within the chamber, means for introducing substantially simultaneously into the at least partially evacuated chamber both a measured quantity of powder and a gas whereby an aerosol is formed within the chamber, said chamber also being provided with aerosol exit means whereby the aerosol may be withdrawn from the chamber.

The chamber may conveniently be of substantially spherical shape. The closure means may be in the form of a one-way valve. Such a valve may be located within a

duct connected to the chamber, said duct providing the aerosol exit means. In the case where the device is in the form of an inhaler, the duct may serve as a mouthpiece. The duct may also be connectable to a pump or other device for forming the at least partial vacuum within the chamber.

The means for introducing substantially simultaneously into the chamber both the powder and a gas may be in the form of a passageway, connected to the chamber, indeed, said passageway may extend from the exterior of the chamber to a position located within the chamber. Where the chamber is of substantially spherical shape, the passageway may extend substantially radially inwardly within said chamber.

Preferably, the passageway has mounted therein means for storing the measured quantity of powder. More preferably the passageway includes passageway closing means operable to allow communication between the interior and exterior of the chamber whereby gas may enter the chamber carrying with it the micronised powder located within the passageway.

The passageway closure means may be in the form of a moveable element which has associated with it the measured dose of powder. Movement of said movable element is effective to open the passageway whereby gas enters the chamber taking with it the measured dose of powder. The moveable element may be of such dimension as to be able to move within the passageway while maintaining sealing contact with the inner walls of the passageway, thereby ensuring that the reduced pressure within the chamber may be maintained until such time as the element reaches the end of its path of travel. At this point the powder is released into the chamber simultaneously with the release of the vacuum in the chamber.

The moveable element may typically be in the form of a spool including enlarged end portions interconnected by an intermediate portion of reduced cross-section. The shape of the moveable element between the end elements may be such that a space of

the desired dose volume is defined between the moveable element and the inner walls of the passageway, in which space the micronised powder is enclosed.

Following production of the aerosol within the chamber, the aerosol is then caused to exit from the chamber. In the case where the device is an inhaler, it may be provided with a mouthpiece within which is located the chamber closure means in the form of a one-way valve. This one-way valve is used both for evacuation of the chamber and also allows inhalation of medicament by the patient. Preferably the one-way valve is located within the mouthpiece.

The present invention also provides a method for producing an aerosol of a micronised powder, said method comprising providing a chamber having openable closure means, operating the closure means to provide at least a partial vacuum within the chamber, introducing substantially simultaneously into the at least partially evacuated chamber both a measured quantity of powder and a gas to form an aerosol within the chamber and withdrawing the aerosol from the chamber via aerosol exit means.

The present invention will now be described, by way of example only, and with reference to the accompanying drawings in which Figures 1 to 3 show the device at various stages in its operation and Figure 4 shows detail of the moveable element of the device of Figures 1 to 3.

Referring to the accompanying drawings, apparatus in accordance with the present invention includes a chamber 1 in the form of a spherical container. Chamber 1 is provided with an opening 2 within which is mounted a one-way valve 3. Extending from opening 2 radially outwardly from the outside surface of chamber 1 is a mouthpiece 4 in the form of a duct which surrounds the main body of one-way valve 3.

Diametrically opposite opening 2, chamber 1 is provided with a further opening 5 within which is mounted powder injector 6. Injector 6 includes a relatively large diameter duct 6a of short length which extends outwardly from opening 5, and a relatively narrow diameter passageway 6b which extends radially inwardly from opening 5. Passageway 6b itself comprises two portions. Portion 6c, extending inwardly from opening 5 is of relatively small internal diameter and is housed within portion 6d, which is of relatively larger diameter and extends inwardly from opening 5 to a position approximately in the centre of the chamber 1 and well beyond the limit of the extension of portion 6c. At its free inner end passageway 6b includes openings through which the powder may enter the chamber 1, but the passageway is at least partially closed by means of end wall 6e.

As shown in Figure 1, there is located within portion 6c and passageway 6b a spool 7 having enlarged ends and an intermediate portion of relatively narrow diameter. Spool 7 and the inner wall portion 6c of passageway 6b together define a space within which is located a micronised powder 8.

To operate the above described device, the line of a vacuum pump is first attached to mouthpiece 4 and the sphere 1 is evacuated to create a vacuum therein. During this operation one-way valve 3 moves away from its seating position on sphere 1 to allow air to be withdrawn from the interior of the sphere. When sufficient vacuum has been created, the pump line is withdrawn and one-way valve 3 now sits firmly on its seat on sphere 1 thereby maintaining the vacuum within the sphere.

The patient then operates a mechanism (not shown) to cause spool 7 to be move from the position shown in Figure 1 to the position shown in Figure 2. As the spool leaves portion 6c of passageway 6c, air is able to enter the sphere via duct 6a and passageway 6b. High speed air flow takes place around spool 7 causing the powder to deagglomorate and be carried in to the main cavity of chamber 1. In so doing it forms an aerosol with the incoming air, as illustrated in Figure 2.

The patient then places mouthpiece 4 in his mouth and inhales causing one-way valve 3 to move to the position shown in Figure 3 and the aerosol is drawn out of the sphere and in to the patient's mouth. This position is illustrated in Figure 3.

CLAIMS

1. A device for producing an aerosol of a micronised powder, said device comprising a chamber having openable closure means operable to allow at least a partial vacuum to be created and maintained within the chamber, means for introducing substantially simultaneously into the at least partially evacuated chamber both a measured quantity of powder and a gas whereby an aerosol is formed within the chamber, said chamber also being provided with aerosol exit means whereby the aerosol may be withdrawn from the chamber.

2. A device according to Claim 1 wherein the chamber is of substantial spherical shape.

3. A device according to Claim 1 or Claim 2 wherein the closure means is in the form of a one-way valve.

4. A device according to Claim 3 wherein said valve is located within a duct connected to the chamber, said duct providing the aerosol exit means.

5. A device according to Claim 4 wherein the device is in the form of an inhaler having a mouthpiece which is provided by the duct.

6. A device according to Claim 5 wherein the duct is adapted to be connectable to a pump or other device for forming the at least partial vacuum within the chamber.

7. A device according to any of the preceding claims wherein the means for introducing substantially simultaneously into the chamber both the powder and a gas is in form of a passageway which is connected to the chamber.

8. A device according to Claim 7 wherein the passageway extends from the exterior of the chamber to a position located within the chamber.

9. A device according to Claim 8 wherein the chamber is of substantially spherical shape and the passageway extends substantially radially inwardly within said chamber.

10. A device according to Claim 8 or Claim 9 wherein the passageway has mounted therein means for storing the measured quantity of powder.

11. A device according to any of Claims 8 to 10 wherein the passageway includes passageway closure means operable to allow communication between the interior and the exterior of the chamber whereby gas may enter the chamber carrying with it the micronised powder located within the passageway.

12. A device according to Claim 11 wherein the passageway closure means is in the form of a moveable element which, in use, has associated with it the measured dose of powder.

13. A device according to Claim 12 wherein the moveable element is of a size and shape such as to be able to move within the passageway while maintaining sealing contact with the inner or walls of the passageway.

14. A device according to Claim 13 wherein the moveable element is in a form of a spool including enlarged end portions interconnected by an intermediate portion of reduced cross-section.

15. A device according to Claim 14 wherein the moveable element is of a size such that a space of the desired dose volume is defined between the moveable element and the inner wall or walls of the passageway, in which space the micronised powder will, in use, be located.

16. A device according to any of the preceding claims in the form of an inhaler provided with a mouthpiece within which is located the chamber closer means in the form of a one-way valve.

17. A method for producing an aerosol of a micronised powder, said method comprising providing a chamber having openable closure means, operating the closure means to provide at least a partial vacuum within the chamber, introducing substantially simultaneously into the at least partially evacuated chamber both a measured quantity of powder and a gas to form an aerosol within the chamber and withdrawing the aerosol from the chamber via aerosol exit means.

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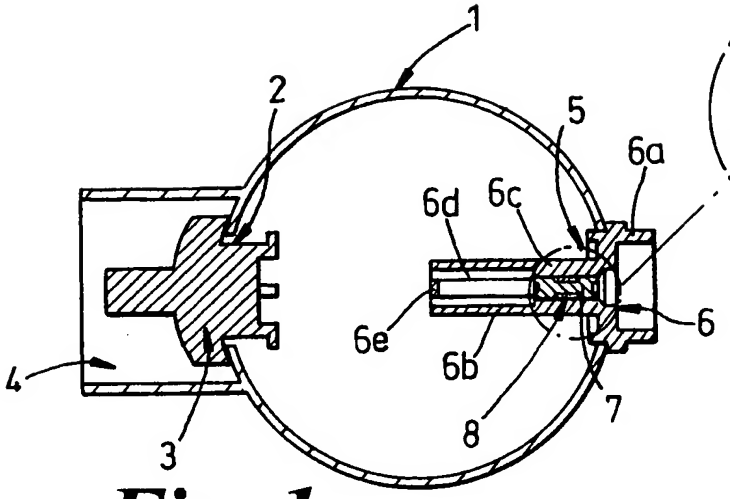

Fig. 1

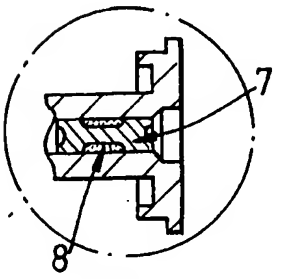

Fig. 4

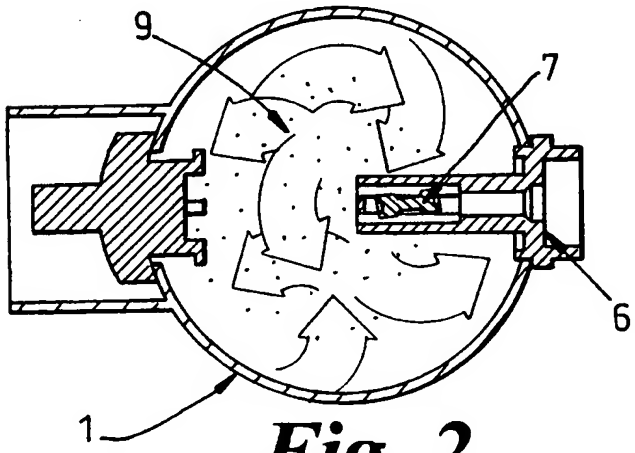

Fig. 2

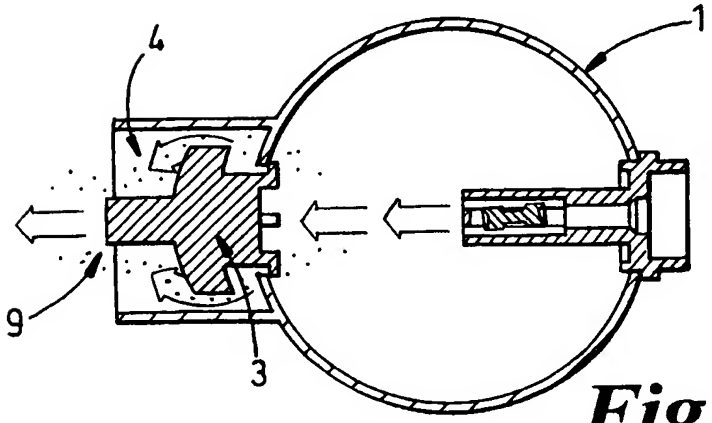

Fig. 3

INTERNATIONAL SEARCH REPORT

Internal Application No
PCT/GB 98/02685

A. CLASSIFICATION OF SUBJECT MATTER
IPC 6 A61M15/00

According to International Patent Classification (IPC) or to both national classification and IPC

B. FIELDS SEARCHED

Minimum documentation searched (classification system followed by classification symbols)
IPC 6 A61M

Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched

Electronic data base consulted during the international search (name of data base and, where practical, search terms used)

C. DOCUMENTS CONSIDERED TO BE RELEVANT

Category °	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	WO 97 01365 A (FISONS PLC ;SHEPHERD MICHAEL TREVOR (GB)) 16 January 1997 see page 9, line 12 - page 11, line 12; figures	1,3-5,7, 8,10,11, 16,17
A	WO 92 04066 A (BISGAARD HANS) 19 March 1992 see abstract; figures	1,17
A	US 5 239 992 A (BEHAR ALAIN ET AL) 31 August 1993 see claim 1; figures 1-3	12,13

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☒ Patent family members are listed in annex.

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